REMARKS

Status of the Claims:

Claims 1-23 are pending. Claims 1, 9 and 15 have been amended to more particularly point out the invention. Support for the amendment to claim 15 is found in the specification on page 45, lines 20-25. Claims 1 and 9 have been amended to recite the SEQ ID NOS of the 3D1 antibody. Support for this amendment is found in figure 1A and 1B. New claims 24 and 25 have been added to more particularly point out the invention. Support for new claim 24 is found in the specification on page 12, lines 13-21. Support for new claim 25 is found in the specification on page 45, lines 15-27.

Written Description Under 35 U.S.C. §112 First Paragraph

Claims 15-23 stand rejected under 35 U.S.C. §112 first paragraph for allegedly failing to comply with the written description requirement. The Office alleges that the disclosure does not reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. The Office believes the specification does not support a B7-2 antibody with higher affinity for B7-2 than CTLA4Ig and a B7-1 antibody with higher affinity for B7-1 than CTLA4Ig. Without acquiescing in the rejection, and for the sole purpose of expediting prosecution, Applicants have amended claim 15 herein to recite that the combination of B7-1 and B7-2 antibodies has a higher affinity for B7-1 and B7-2 respectively than hCTLA4Ig alone has for both molecules. Claims 16-23 depend on claim 15. Applicants respectfully submit the amendment obviates the rejection.

Enablement Under 35 U.S.C. §112 First Paragraph

Claims 1-23 stand rejected under 35 U.S.C. §112 first paragraph for allegedly failing to comply with the enablement requirement. The Office alleges that the 3D1 antibody is a required element of the claimed invention and therefore must be readily available to the public or obtainable by a repeatable method set forth in the specification.

Applicants note that claims 15-23 do not recite the 3D1 antibody. Applicants submit that the 3D1 antibody is not required to either make or use the subject matter recited in these claims. Accordingly, Applicants respectfully request withdrawal of the enablement rejection with respect to claims 15-23.

Turning to the remaining claims, while claim 1, and its dependencies do recite the 3D1 antibody, Applicants believe these claims are enabled because the 3D1 antibody was known in the art at the time the application was filed (see, e.g., WO 95/03408; U.S. Patent Application No.: 08/101,624). Moreover, both the heavy chain and light chain variable regions of the 3D1 antibody are disclosed in the specification (see, e.g., Figure 1A and 1B; SEQ ID NOS: 1, 2, 3, and 4; page 4, lines 9-12). Applicants submit herewith the entire nucleotide and amino acid sequence of the 3D1 antibody, including the constant regions, thereby making it readily available to the public. See, e.g., Kabat, E.A. et al., *Sequences of Proteins of Immunological Interest*, Fifth Edition, U.S. Department of Health and Human Services, U.S. Government Printing Office, 1991. Applicants believe this submission obviates the enablement rejection with respect to claims 1-14.

Indefiniteness Under 35 U.S.C. §112 Second Paragraph

Claims 1-23 stand rejected under 35 U.S.C. §112 second paragraph as allegedly being indefinite. The Office alleges that the claims recite the 3D1 antibody and that its characteristics are unknown because "3D1" is merely a laboratory designation which does not clearly define the claimed product. As set forth above, claims 15-23 do not recite the term "3D1." Accordingly, Applicants respectfully request withdrawal of this rejection with respect to claims 15-23. Claim 1 does recite the term "3D1," and claims 2-14 depend on claim 1. Applicants believe the term "3D1," is not indefinite because it was used in the art to describe a specific monoclonal antibody. References disclosing the antibody have been incorporated by reference into the specification (see, e.g., page 16, lines 15-24 and page 52, lines 23-24). Nonetheless, for the sole purpose of expediting prosecution, Applicants submit herewith the entire nucleotide and amino acid sequence of the 3D1 antibody and amend claim 1 to recite SEQ ID NOS: 2 and 4. Applicants believe this amendment obviates the rejection.

Anticipation Under 35 U.S.C. §102

Claims 1-3, 6-7 and 20-23 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by WO 95/34320 (hereinafter "Blazar"). The Office alleges that the broadest reasonable interpretation of the term "competes with the murine antibody 3D1 for binding to B7-2" reads on the inhibitory anti-B7-2 antibodies of Blazar because such costimulatory inhibitory agents would have the property of competing with the 3D1 antibody given that the Blazar antibodies allegedly appear to have the same, or nearly the same inhibitory properties. Applicants respectfully traverse this rejection.

The standard for anticipation under 35 U.S.C. § 102 is stated in MPEP § 2131 (emphasis added). "'A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.' *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). 'The identical invention must be shown in as complete detail as is contained in the . . . claim'. *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989)."

Claims 15-17 and 20-23

With respect to claims 15-17 and 20-23, Applicant note that these claims do not recite "competes with the murine antibody 3D1 for binding to B7-2." Claim 15, as amended herein recites: "contacting the donor cells with a combination comprising an immunoglobulin specific to B7-1 and an immunoglobulin specific to B7-2, wherein the combination has a higher affinity for B7-2 than hCTLA4Ig the combination has a higher affinity for B7-1 than hCTLA4Ig." Nothing in Blazar teaches or suggests the B7-1 and B7-2 antibodies recited in claim 15. Claims 16-17 and 20-23 depend on claim 15. Applicants submit that these claims are not anticipated, either expressly or inherently, by Blazar because Blazar does not teach or suggest all of the limitations of these claims. Accordingly, Applicants respectfully request that the rejection of claims 15-17 and 20-23 under 35 U.S.C. §102(b) be withdrawn.

Claims 1-3 and 6-14

With respect to claims 1-3 and 6-14, the Office alleges that because both the claimed B7-2 antibody and the B7-2 antibody disclosed in Blazar both share certain

inhibitory properties they must compete with the 3D1 antibody. There is nothing of record to support this allegation. Applicants note that the 3D1 antibody is specific to human B7-2 (see WO 95/03408, page 31, lines 10-15; page 91, lines 5-20)(courtesy copy enclosed). Applicants further note that Blazar made no B7-2 specific antibodies, but rather relied on B7-2 antibodies produced by others (see, e.g., Blazar, page 36, lines 21-35; page 27, lines 19-20). The GL-1 antibody, used by Blazar in his experiments, is described in Hathcock et al., 1993, *Science* 262:905 (courtesy copy enclosed). Importantly, this antibody recognizes murine B7-2, not human. There is no reason to believe it could therefore compete with the 3D1 antibody because the two antibodies were generated against antigens from different species. The antibodies are thus different and Blazar does not anticipate. Moreover, any generic disclosure in Blazar, of any B7-2 antibody to inhibit a costimulatory signal is merely a wish, and thus not enabled.

Obviousness Rejection Under 35 U.S.C. § 103

Claims 1-11 stand rejected as being obvious in light of Blazar alone, or in combination with U.S. Patent No. 6,096,537 (hereinafter, "Chappel"), U.S. Patent No. 6,096,537 (hereinafter, "Dinsmore") and Goldberg et al. 1994, *Transplant Immunology* 2:27 (hereinafter, "Goldberg"). The Office alleges first that the pending claims, with the amendments filed on March 8, 2004, are obvious in light of Blazar alone because the broadest reasonable interpretation of the term "competes with the murine antibody 3D1 for binding to B7-2" reads on the inhibitory anti-B7-2 antibodies of Blazar because such costimulatory inhibitory agents would have the property of competing with the 3D1

antibody given that the Blazar antibodies allegedly appear to have the same, or nearly the same inhibitory properties. Additionally, the Office reiterates the previous obviousness rejections based on Blazar combined with Chappel, Dinsmore, and Goldberg. The Office alleges that Dinsmore provides motivation and reasonable expectation of success for providing an inhibitory antibody to achieve the desired immunosuppressive effect. The Office also alleges that Goldberg teaches the pretreatment of renal transplants with inhibitory antibodies to prolong survival and that the antibodies can be administered ex vivo. The Office further alleges that Chappel teaches that antibody pretreatment serves to inhibit rejection of transplanted cells or tissues. Applicants maintain that the rejection is in error and respectfully request that it be withdrawn for the reasons stated below.

The Claimed Invention Is Not Prima Facie Obvious

MPEP § 2143 provides the standard required to establish a prima facie case of obviousness. "First there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references combined) must teach or suggest all the claim limitations."

The reasonable expectation of success must be found in the prior art, not in the applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). The references must be considered as a whole and must suggest the desirability, and thus the obviousness of making the combination. *Hodosh v. Block*

Drug Co., Inc., 786 F.2d 1136, 1143 n.5, 229 U.S.P.Q. 182, 187 n.5 (Fed. Cir. 1986); MPEP § 2141. The Patent and Trademark Office (PTO) bears the burden of initially establishing a prima facie case of obviousness. MPEP § 2142.

The PTO has not established that the claimed invention is prima facie obvious in light of the teachings of Blazar alone. Blazar does not teach or suggest all of the claim limitations. Chappel, Dinsmore and Goldberg add nothing to cure this defect.

The Invention Is Not Obvious In Light of Blazar Alone

Blazar neither discloses or suggests a method of transplanting cells which requires contacting the donor cells with an immunoglobulin specific to B7-1, an immunoglobulin specific to B7-2, wherein the immunoglobulin specific to B7-2 can compete with the murine antibody 3D1 for binding to B7-2. Thus Blazar, alone, does not teach or suggest all of the claim limitations. Moreover, because the antibody used in Blazar recognized murine and not human B7-2 there would be no reasonable expectation that the Blazar antibody would successfully compete with the 3D1 antibody which specifically recognizes human B7-2. Accordingly, Applicants submit that the invention is not obvious in light of Blazar alone.

Blazar Combined With Chappel, Dinsmore and Goldberg

The Office alleges that Chappel, Dinsmore or Goldberg provide motivation and reasonable expectation of success, in combining the B7-2 antibodies of Blazar as immuno-inhibtory agents. Blazar combined with Chappel, Dinsmore and Goldberg does not render the claimed invention obvious because the combined references do not teach or suggest all of the claim limitations. First, neither Chappel, Dinsmore or

Goldberg teach or suggest an antibody specific to B7-2 that can compete with the murine antibody 3D1 for binding to B7-2. Thus, the combined references do not cure the defect described above regarding Blazar. Moreover, none of the cited references provide any reasonable expectation that an antibody specific to murine B7-2, as used in Blazar, could compete with the 3D1 antibody which recognizes human B7-2. Accordingly, Applicants submit that the invention is not prima facie obvious. Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this filing and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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